

HEPATITIS A, 1995: OLD AND NEW PROBLEMS

WE HATE TO BOAST, but in 1995, Oregon had the highest rate of hepatitis A in the nation. The 2,956 cases reported in 1995 smashed our previous record (2,366 cases in 1989) by 25%. The cumulative rate for the year was 94 cases/100,000 population; this compares with a nationwide rate of about 11 cases/100,000. Linn, Douglas, and Lane Counties each had rates of more than 200/100,000 (map, *verso*). Statewide, persons aged 20-39 years had the highest rate: 182 cases/100,000. Two deaths were reported.

Humans are the only important reservoir for hepatitis A virus (HAV); it is spread from person to person through the fecal-oral route. The vast majority of recognized cases were sporadic and did not occur as part of a cluster. Although there were many public announcements regarding cases of hepatitis A in food handlers, only one point-source outbreak of hepatitis A was recognized in Oregon in the past year, perhaps because of the education of cases and the diligent administration of prophylactic immune globulin by county health nurses to household and day care contacts of cases. (The one cluster resulted from exposure to a case who was undiagnosed because he had not sought medical care.) As part of routine case investigations, county public health nurses ask about illicit drug use, which has been associated with hepatitis A in the past.¹ In 1995,

such use was reported among 503 (17%) of our 2,956 total cases but among 397 (24%) of the 1,656 cases in the 20-39 year age group. Hepatitis A is rarely blood-borne, and drug use is more likely a marker for poor hygiene than a direct mode of transmission. Improving the hygiene of this population has proved difficult.

HEPATITIS A VACCINE

Havrix® is an inactivated hepatitis A vaccine, manufactured by SmithKline Beecham and licensed by the U.S. Food and Drug Administration on February 22, 1995. Recommended dosing schedules are shown in the Table. This vaccine produced seroconversion rates of 95-100% after one month,²⁻⁴ and it provided 94% (95% CI, 79%-99%) protection against hepatitis A in a large, controlled trial among schoolchildren in Thailand.²

At-risk populations for whom vaccination against hepatitis A should be considered include:⁵

1. Persons traveling to or working in countries with high or intermediate endemicity of infection, including countries in Central and South America, southern and eastern Europe, Africa, and Asia (excepting Japan). For short-term travelers, immunoglobulin (IG) may suffice; but persons traveling repeatedly or for periods longer than 5 months may be better served by vaccination. Vaccinees can be assumed to be protected by four weeks after receiving the initial dose. Those leaving in a hurry should consider receiving prophylactic IG in addition to vaccine.
2. Children in communities with high rates of HAV infection and periodic hepatitis A outbreaks. These include native American communities.
3. Men who have sex with men.⁶
4. Illicit drug users.
5. Persons who work with HAV in a laboratory or with HAV-infected primates.

6. Persons with chronic liver disease, since they may be more likely to develop complications with hepatitis A.
7. Persons receiving clotting factor concentrate. Since the intramuscular injections may produce bleeding, the vaccine can be given shortly after receipt of the clotting factor.

Age (years)	Dose (intramuscular)	Schedule (months)
2-18	360 EL.U. in 0.5 ml	0, 1, and 6-12
≥19	1440 EL.U. in 1 ml	0 and 6-12

Since immunity following hepatitis A is life-long, persons with past infection need not be vaccinated. The prevalence of antibodies to HAV increases with age. During 1976-1980, a nationwide serosurvey found that 11% of children <5 years old and 74% of adults ≥50 years old had anti-HAV antibodies. Prevalences among males and females were similar. Fifty percent of persons who reported an annual income of <\$10,000 were seropositive, compared with only 26% among those with annual incomes of >\$25,000. Testing for pre-existing antibodies in members of high-prevalence groups may save the cost of an expensive vaccine.

HEPATITIS A AND CLOTTING FACTOR CONCENTRATES

The Centers for Disease Control and Prevention (CDC) reported 3 cases of hepatitis A in the United States during September-November, 1995, among recipients of Alphanate™ (a brand of factor VIII concentrate), lot number AP2014A. Polymerase chain reaction (PCR)-amplified HAV sequences from one patient's serum, from one patient's stool, and from the implicated lot of Alphanate™ were identical. In addition, a patient with hemophilia B (factor IX deficiency; Christmas disease) contracted hepatitis A in December 1995; some of the AlphaNine S-D™ (brand of factor IX concentrate) that he had received during the preceding 3 months originated from source plasma pools common to

the implicated lot of Alphanate™.⁷ Both Alphanate™ and AlphaNine S-D™ are treated using the solvent-detergent (S-D) method. Clotting factors made with recombinant technology have not been shown to transmit any infectious agents, but no recombinant factor IX has yet been approved by FDA.

CDC is requesting assistance in identifying additional cases. Patients who received Alphanate™ lot numbers CA5410A, CA5412A, CA5413A, or AlphaNine S-D™ lot number CA5421A since July 1, 1995, should be tested for IgM anti-HAV. Patients who are IgM anti-HAV positive should be reported to their local health departments.

The Hemophilia Center at the Oregon Health Sciences University currently follows 237 patients with hemophilia: 154 with hemophilia A, 46 with hemophilia B, and 37 with von Willebrand's disease. Alphanate™ is not widely used in Oregon. Hemophilia Center officials know of 14 patients with hemophilia B who have used AlphaNine S-D™ since July 1. Hepatitis A serologies are routinely checked at the Hemophilia Center, and patients are being called to determine whether any have been ill since July 1995.

In addition to the recently reported U.S. cases, 52 cases of hepatitis A among hemophiliacs in Italy during 1989-1992

were associated with receiving factor VIII concentrates treated with the S-D method. PCR-amplified RNA sequences from patient sera matched those from factor VIII concentrates. Hepatitis A infections have also been reported from hemophiliacs in Germany, Ireland, and Belgium, who had received similar preparations of factor VIII concentrate.⁸

Efforts to protect the blood supply have centered on disrupting the envelopes that are present on hepatitis B and C viruses and on HIV, using S-D methods. HAV, having no envelope, is not susceptible to inactivation using S-D methods. Physicians should consider vaccinating susceptible patients, i.e., those without pre-existing anti-HAV antibody, who receive clotting factor concentrates, with inactivated hepatitis A vaccine.

REFERENCES

- Schade CP, Komorowska D. Continuing outbreak of hepatitis A linked with intravenous drug abuse in Multnomah County. *Public Health Rep* 1988; 103:452-9.
- Innis BL, Snitbhan R, Kunasol P, et al. Protection against hepatitis A by an inactivated vaccine. *JAMA* 1994; 271:1328-34.
- McMahon BJ, Williams J, Bulkow L, et al. Immunogenicity of an inactivated hepatitis A vaccine in Alaska native children and native and non-native adults. *J Infect Dis* 1995; 171:676-9.
- Clemens R, Safary A, Hepburn A, Roche C, Stanbury WJ, André FE. Clinical experience with an inactivated hepatitis A vaccine. *J Infect Dis* 1995; 171(Suppl 1):S44-9.
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- Centers for Disease Control and Prevention. Hepatitis A among persons with hemophilia who received clotting factor concentrate - United States, September-December 1995. *MMWR* 1996; 45:29-32.

- Mannucci PM, Gdovin S, Gringeri A, et al. Transmission of hepatitis A to patients with hemophilia by factor VIII concentrates treated with organic solvent and detergent to inactivate viruses. *Ann Intern Med* 1994; 120:1-7.

County Rabies Contacts

THE FOLLOWING CONTACTS should be added to the list published in the January 23rd issue:

Corrections:

Clackamas: 655-8384
Wasco-Sherman: John Zalaznik, ST
Washington: 681-7041

Addition:

Union: Midge Vogan, 962-8825.

Measles at Blazers Game

ASPECTATOR at the January 29 Trail Blazers-Sonics game at the Rose Garden (Sonics 92, Blazers 88) has been diagnosed with measles pneumonia. Measles is highly contagious; an athlete with measles transmitted the illness to 16 others at the Metrodome (capacity: 55,000) in Minnesota in 1991.¹ We ask that all health care practitioners be alert to symptoms of measles in sports fans presenting through February 16.

Symptoms of measles include cough, coryza, conjunctivitis, fever, malaise, photophobia, nasal congestion, lymphadenopathy, and Koplik spots, before the onset of the maculopapular rash. Laboratory confirmation is strongly recommended.

Anyone born since January 1, 1957 should receive two doses of measles vaccine, a minimum of 30 days apart.

REFERENCE

- Ehresmann KR, Hedberg CW, Grimm MB, Norton CA, MacDonald KL, Osterholm MT. An outbreak of measles at an international sporting event with airborne transmission in a domed stadium. *J Infect Dis* 1995; 171:679-83.